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(FILE 'HOME' ENTERED AT 13:09:36 ON 22 APR 2002)

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FILE 'MEDLINE, AGRICOLA, CANCERLIT, SCISEARCH, CAPLUS, BIOSIS, MEDICONF'
     ENTERED AT 13:09:45 ON 22 APR 2002
         756977 S CHROMOSOME?
L1
            301 S L1 AND (INTRON? (L) ENDONUCLEASE?)
L2
            137 DUP REM L2 (164 DUPLICATES REMOVED)
L3
            137 FOCUS L3 1-
1.4
            153 S L1 AND ((GROUP I INTRON?) OR (INTRON ENCODED))
L5
            77 S L5 (L) ENDONUCLEASE?
L6
            77 S L5 AND ENDONUCLEASE?
L7
            37 DUP REM L7 (40 DUPLICATES REMOVED)
T.B
             37 SORT L8 PY
L9
            37 FOCUS L9 1-
L10
              2 S L9 AND MAMMAL?
T.1.1
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L12
             82 DUP REM L12 (132 DUPLICATES REMOVED)
L13
             82 FOCUS L13 1-
1.14
             25 S L13 AND MAMMAL?
1.15
             25 SORT L15 PY
L16
=> d an ti so au ab pi 114 1 9 11 12 16
L14 ANSWER 1 OF 82 CAPLUS COPYRIGHT 2002 ACS
     1998:545391 CAPLUS
DN
     129:172448
     Cloning and expression of gene for restriction endonuclease I-
     SceI of Saccharomyces cerevisiae and use of I-
     U.S., 79 pp. Cont.-in-part of U.S. 5,474,896.
     CODEN: USXXAM
     Dujon, Bernard; Choulika, Andre; Perrin, Arnaud; Nicolas, Jean-francois
TN
     A mitochondrial gene encoding restriction endonuclease I-
     SceI of Saccharomyces cerevisiae and a synthetic universal code
     encoding I-SceI for the expression in Escherichia coli
     and yeast are provided. Applications of I-SceI for
     genetically mapping yeast chromosomes by the nested chromosomal
     fragmentation strategy, inducing double stranded DNA break, and in vivo
     site-directed insertion of genes and homologous recombination in
     eukaryotes are also described. It may also be used for prepg. transgenic
     animal models of human diseases and genetic disorders.
                     KIND DATE
                                          APPLICATION NO. DATE
     PATENT NO.
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                                          US 1994-336241
                                                           19941107
PΤ
     US 5792632
                      A
                            19980811
                                           US 1992-971160
                                                           19921105
     US 5474896
                      Α
                            19951212
                                          US 1995-465273
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     US 5866361
                      Α
                            19990202
                      AA 19960517
                                          CA 1995-2203569 19951106
     CA 2203569
                           19960517
                                          WO 1995-EP4351
                                                          19951106
     WO 9614408
                      A2
                            19960829
     WO 9614408
                       A3
         W: CA, JP
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                      A1 19970827
                                         EP 1995-938418 19951106
     EP 791058
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                                                          19951106
                                          JP 1995-515058
     JP 10508478
                       T2 19980825
                            19990907
                                          US 1998-119024
     US 5948678
                       Α
L14 ANSWER 9 OF 82
                       MEDLINE
                MEDLINE
     95140628
     Repair of a specific double-strand break generated within a mammalian
     chromosome by yeast endonuclease I-SceI.
     NUCLEIC ACIDS RESEARCH, (1994 Dec 25) 22 (25) 5649-57.
SO
     Journal code: O8L; 0411011. ISSN: 0305-1048.
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SK1636

Lukacsovich T; Yang D; Waldman A S

AU

We established a mouse Ltk- cell line that contains within its genome a herpes simplex virus thymidine kinase gene (tk) that had been disrupted by the insertion of the recognition sequence for yeast endonuclease I -SceI. The artificially introduced 18 bp I-SceI recognition sequence was likely a unique sequence in the genome of the mouse cell line. To assess whether an induced double-strand break (DSB) in the genomic tk gene would be repaired preferentially by gene targeting or non-homologous recombination, we electroporated the mouse cell line with endonuclease I-SceI alone, one of two different gene targeting constructs alone, or with I-SceI in conjunction with each of the two targeting constructs. Each targeting construct was, in principle, capable of correcting the defective genomic tk sequence via homologous recombination. tk+ colonies were recovered following electroporation of cells with I-SceI in the presence or absence of a targeting construct. Through the detection of small deletions at the I-SceI recognition sequence in the mouse genome, we present evidence that a specific DSB can be introduced into the genome of a living mammalian cell by yeast endonuclease I-SceI. We further report that a DSB in the genome of a mouse Ltk- cell is repaired preferentially by non-homologous end-joining rather than by targeted homologous recombination with an exogenous donor sequence. The potential utility of this system is discussed.

L14 ANSWER 11 OF 82 MEDLINE

AN 92123196 MEDLINE

- TI Complex recognition site for the group I intron-encoded endonuclease I-SceII.
- SO MOLECULAR AND CELLULAR BIOLOGY, (1992 Feb) 12 (2) 716-23.

  Journal code: NGY: 8109087. ISSN: 0270-7306.
- AU Wernette C; Saldanha R; Smith D; Ming D; Perlman P S; Butow R A
- We have characterized features of the site recognized by a double-stranded DNA endonuclease, I-SceII, encoded by intron 4 alpha of the yeast mitochondrial COX1 gene. We determined the effects of 36 point mutations on the cleavage efficiency of natural and synthetic substrates containing the Saccharomyces capensis I-SceII site. Most mutations of the 18-bp I-SceII recognition site are tolerated by the enzyme, and those mutant sites are cleaved between 42 and 100% as well as the wild-type substrate is. Nine mutants blocked cleavage to less than or equal to 33% of the wild-type, whereas only three point mutations, G-4----C, G-12----T, and G-15----C, block cleavage completely. Competition experiments indicate that these three substrates are not cleaved, at least in part because of a marked reduction in the affinity of the enzyme for those mutant DNAs. About 90% of the DNAs derived from randomization of the nucleotide sequence of the 4-bp staggered I-SceII cleavage site are not cleaved by the enzyme. I-SceII cleaves cloned DNA derived from human chromosome 3 about once every 110 kbp. The I-SceII recognition sites in four randomly chosen human DNA clones have 56 to 78% identity with the 18-bp site in yeast mitochondrial DNA; they are cleaved at least 50% as well as the wild-type mitochondrial substrate despite the presence of some substitutions that individually compromise cleavage of the mitochondrial substrate. Analysis of these data suggests that the effect of a given base substitution in I-SceII cleavage may depend on the sequence at other positions.

L14 ANSWER 12 OF 82 CAPLUS COPYRIGHT 2002 ACS

AN 2000:553718 CAPLUS

DN 133:160582

- Gene repair involving homologous recombination induced by in vivo double-stranded cleavage of targeting DNA mediated by chimeric restriction endonuclease
- SO PCT Int. Appl., 38 pp. CODEN: PIXXD2
- IN Choulika, Andre; Mulligan, Richard C.
- AB Methods of modifying, repairing, attenuating and inactivating a gene or other chromosomal DNA in a cell through chimeric restriction endonuclease (or meganuclease)-induced homologous recombination are disclosed. 101The method is exemplified by introducing into a cell a vector contg. a targeting DNA homologous to a chromosomal target sites and is flanked by

specific sites for restriction endonuclease I-SceI (a Saccharomyces cerevisiae intron-encoded rare-cutter endonuclease recognizing 18-bp sequence) or meganuclease, and cDNA encoding I -SceI or meganuclease. The I-SceI site is recognized and cleaved in vivo to relase the repair matrix and induce homologous recombination. The method has applications in treating or prophylaxis of a genetic disease in an individual in need. APPLICATION NO. DATE KIND DATE PATENT NO. \_\_\_\_ WO 2000046386 A2 20000810 WO 2000-US3014 20000203 WO 2000046386 A3 20001214 W: AU, CA, JP, US RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE EP 2000-908499 20000203 20011024 EP 1147209 A2 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,

- IE, FI
  L14 ANSWER 16 OF 82 MEDLINE
- AN 95198715 MEDLINE

PΙ

- TI Induction of homologous recombination in mammalian chromosomes by using the I-SceI system of Saccharomyces
- SO MOLECULAR AND CELLULAR BIOLOGY, (1995 Apr) 15 (4) 1968-73. Journal code: NGY; 8109087. ISSN: 0270-7306.
- AU Choulika A; Perrin A; Dujon B; Nicolas J F
- The mitochondrial intron-encoded endonuclease I-SceI AB of Saccharomyces cerevisiae has an 18-bp recognition sequence and, therefore, has a very low probability of cutting DNA, even within large genomes. We demonstrate that double-strand breaks can be initiated by the I-SceI endonuclease at a predetermined location in the mouse genome and that the breaks can be repaired with a donor molecule homologous regions flanking the breaks. This induced homologous recombination is approximately 2 orders of magnitude more frequent than spontaneous homologous recombination and at least 10 times more frequent than random integration near an active promoter. As a consequence of induced homologous recombination, a heterologous novel sequence can be inserted at the site of the break. This recombination can occur at a variety of chromosomal targets in differentiated and multipotential cells. These results demonstrate homologous recombination involving chromosomal DNA by the double-strand break repair mechanism in mammals and show the usefulness of very rare cutter endonucleases, such as I-SceI, for designing genome rearrangements.

## => d an ti so au ab pi 116 2 4 5 8

- L16 ANSWER 2 OF 25 MEDLINE
- AN 95140628 MEDLINE
- TI Repair of a specific double-strand break generated within a mammalian chromosome by yeast endonuclease I-SceI.
- SO NUCLEIC ACIDS RESEARCH, (1994 Dec 25) 22 (25) 5649-57. Journal code: O8L; 0411011. ISSN: 0305-1048.
- AU Lukacsovich T; Yang D; Waldman A S
- We established a mouse Ltk- cell line that contains within its genome a herpes simplex virus thymidine kinase gene (tk) that had been disrupted by the insertion of the recognition sequence for yeast endonuclease I -SceI. The artificially introduced 18 bp I-SceI recognition sequence was likely a unique sequence in the genome of the mouse cell line. To assess whether an induced double-strand break (DSB) in the genomic tk gene would be repaired preferentially by gene targeting or non-homologous recombination, we electroporated the mouse cell line with endonuclease I-SceI alone, one of two different gene targeting constructs alone, or with I-SceI in conjugation with each of the two targeting constructs

SceI in conjunction with each of the two targeting constructs. Each targeting construct was, in principle, capable of correcting the defective genomic tk sequence via homologous recombination. tk+ colonies were recovered following electroporation of cells with I-

SceI in the presence or absence of a targeting construct. Through

the detection of small deletions at the I-SceI recognition sequence in the mouse genome, we present evidence that a specific DSB can be introduced into the genome of a living mammalian cell by yeast endonuclease I-SceI.

We further report that a DSB in the genome of a mouse Ltk- cell is repaired preferentially by non-homologous end-joining rather than by targeted homologous recombination with an exogenous donor sequence. The potential utility of this system is discussed.

- L16 ANSWER 4 OF 25 CAPLUS COPYRIGHT 2002 ACS
- AN 1995:534146 CAPLUS
- DN 123:134052
- TI The yeast I-SceI meganuclease induces site-directed chromosomal recombination in mammalian cells
- SO C. R. Acad. Sci., Ser. III (1994), 317(11), 1013-9 CODEN: CRASEV: ISSN: 0764-4469
- AU Choulika, Andre; Perrin, Arnaud; Dujon, Bernard; Nicolas, Jean-Francois
- Double-strand breaks in genomic DNA stimulate recombination. Until now it was not possible to induce in vivo site-directed double-strand breaks in a mammalian chromosomal target. In this article the authors describe the use of I-SceI meganuclease, a very rare cutter yeast endonuclease, to induce site-directed double-strand breaks mediated recombination. The results demonstrate the potential of the I-SceI system for chromosome manipulation in mammalian cells.
- L16 ANSWER 5 OF 25 MEDLINE
- AN 95198715 MEDLINE
- TI Induction of homologous recombination in mammalian chromosomes by using the I-SceI system of Saccharomyces cerevisiae.
- SO MOLECULAR AND CELLULAR BIOLOGY, (1995 Apr) 15 (4) 1968-73.

  Journal code: NGY; 8109087. ISSN: 0270-7306.
- AU Choulika A; Perrin A; Dujon B; Nicolas J F
- The mitochondrial intron-encoded endonuclease I-SceI AB of Saccharomyces cerevisiae has an 18-bp recognition sequence and, therefore, has a very low probability of cutting DNA, even within large genomes. We demonstrate that double-strand breaks can be initiated by the I-SceI endonuclease at a predetermined location in the mouse genome and that the breaks can be repaired with a donor molecule homologous regions flanking the breaks. This induced homologous recombination is approximately 2 orders of magnitude more frequent than spontaneous homologous recombination and at least 10 times more frequent than random integration near an active promoter. As a consequence of induced homologous recombination, a heterologous novel sequence can be inserted at the site of the break. This recombination can occur at a variety of chromosomal targets in differentiated and multipotential cells. These results demonstrate homologous recombination involving chromosomal DNA by the double-strand break repair mechanism in mammals and show the usefulness of very rare cutter endonucleases, such as I -SceI, for designing genome rearrangements.
- L16 ANSWER 8 OF 25 CAPLUS COPYRIGHT 2002 ACS
- AN 1996:428575 CAPLUS
- DN 125:107019
- TI Nucleotide sequence encoding yeast enzyme I-SceI and its use in inducing homologous recombination in eukaryotic cells and protein production in transgenic animals
- SO PCT Int. Appl., 122 pp. CODEN: PIXXD2
- IN Choulika, Andre; Perrin, Arnaud; Dujon, Bernard; Nicolas, Jean-Francois
- AB Synthetic DNA encoding the enzyme I-SceI is provided.

  The DNA sequence can be incorporated in cloning and expression vectors, transformed cell lines and transgenic animals. The vectors are useful in gene mapping and site-directed insertion of genes. A synthetic gene encoding Saccharomyces cerevisiae I-SceI restriction endonuclease was expressed in Escherichia coli and yeast. The enzyme was used in genetic mapping of a yeast chromosome, of YAC's, and of cosmids. I-SceI efficiently induced double-stranded breaks in a chromosomal target in mammalian cells and the breaks

were repaired using a donor mol. that shares homol. with the regions flanking the break.

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|----|-------------------|---------------------|--------------------|----------------------|
|    | PATENT NO.        | KIND DATE           | APPLICATION NO.    | DATE                 |
|    |                   |                     |                    |                      |
| ΡI | WO 9614408        | A2 19960517         | WO 1995-EP4351     | 19951106             |
|    | WO 9614408        | A3 19960829         |                    |                      |
|    | W: CA, JP         |                     |                    |                      |
|    | RW: AT, BE, C     | CH, DE, DK, ES, FR, | GB, GR, IE, IT, LU | , MC, NL, PT, SE     |
|    | US 5792632        | A 19980811          | US 1994-336241     |                      |
|    | EP 791058         | A1 19970827         | EP 1995-938418     |                      |
|    | R: AT, BE, C      | CH, DE, DK, ES, FR, | GB, GR, IE, IT, LI | , LU, MC, NL, PT, SE |
|    | JP 10508478       | T2 19980825         | JP 1995-515058     | 19951106             |

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SK1636

(FILE 'HOME' ENTERED AT 13:09:36 ON 22 APR 2002)

FILE 'MEDLINE, AGRICOLA, CANCERLIT, SCISEARCH, CAPLUS, BIOSIS, MEDICONF' ENTERED AT 13:09:45 ON 22 APR 2002 756977 S CHROMOSOME? 301 S L1 AND (INTRON? (L) ENDONUCLEASE?)  $L_2$ 137 DUP REM L2 (164 DUPLICATES REMOVED) L3 137 FOCUS L3 1-Ľ4 153 S L1 AND ((GROUP I INTRON?) OR (INTRON ENCODED)) L5 77 S L5 (L) ENDONUCLEASE? L6 77 S L5 AND ENDONUCLEASE? L7 37 DUP REM L7 (40 DUPLICATES REMOVED) 1.8 L9 37 SORT L8 PY 37 FOCUS L9 1-L10 2 S L9 AND MAMMAL? 1.11 => d an ti so au ab 111 1-2 L11 ANSWER 1 OF 2 MEDLINE 95198715 MEDLINE Induction of homologous recombination in mammalian ΤT chromosomes by using the I-SceI system of Saccharomyces MOLECULAR AND CELLULAR BIOLOGY, (1995 Apr) 15 (4) 1968-73. Journal code: NGY; 8109087. ISSN: 0270-7306. Choulika A; Perrin A; Dujon B; Nicolas J F AII The mitochondrial intron-encoded endonuclease I-SceI of Saccharomyces cerevisiae has an 18-bp recognition sequence and, therefore, has a very low probability of cutting DNA, even within large genomes. We demonstrate that double-strand breaks can be initiated by the I-SceI endonuclease at a predetermined location in the mouse genome and that the breaks can be repaired with a donor molecule homologous regions flanking the breaks. This induced homologous recombination is approximately 2 orders of magnitude more frequent than spontaneous homologous recombination and at least 10 times more frequent than random integration near an active promoter. As a consequence of induced homologous recombination, a heterologous novel sequence can be inserted at the site of the break. This recombination can occur at a variety of chromosomal targets in differentiated and multipotential cells. These results demonstrate homologous recombination involving chromosomal DNA by the double-strand break repair mechanism in mammals and show the usefulness of very rare cutter endonucleases, such as I-SceI, for designing genome rearrangements. L11 ANSWER 2 OF 2 CANCERLIT 96605697 CANCERLIT AN Repair of DNA double strand breaks in mammalian cells by homologous recombination and end-joining mechanisms (Meeting abstract). J Cell Biochem, (1995). Suppl. 21A, pp. 328. SO ISSN: 0730-2312. Jasin M; Rouet P; Smih F ΑU To study the repair of DSBs introduced into mammalian chromosomal DNA, we have developed expression vectors for rare-cutting, site-specific endonucleases from S cerevisiae. We used the universal code equivalent of the mitochondrial intronencoded endonuclease I-Sce I to build the mammalian expression vector, pCMV-I-Sce I. The I-Sce I sequence was provided by B Dujon, Pasteur Institute. In addition to providing a consensus Kozak sequence for efficient translation, the I-Sce I ORF was modified by fusing sequences encoding a nuclear localization signal and a hemagglutinin epitope tag. Our initial assay for in vivo cutting and enhanced recombination measures extrachromosomal recombination, since this form of recombination is very efficient in mammalian cells and sensitive to DSBs. The assay utilizes RSVCAT plasmid substrates consisting

of overlapping chloramphenical acetyltransferase (CAT) gene fragments transiently transfected into cells. The RSVCAT plasmids were modified by the insertion of a synthetic I-Sce I site at the end of the homology repeats and cotransfections were carried out in COS 1 cells. We observed a substantial increase of CAT activity in cotransfections of pCMV-I-Sce I

with CAT substrates containing the I-Sce I site but not with plasmids lacking the site. Southern analysis verified in vivo cleavage, as well as recombination. Constitutive expression of the endonuclease is not toxic to mouse 3T3 cells. These results have been recently published (Rouet P et al, Proc Natl Acad Sci; 91:6064 1994). We have recently observed efficient cutting of introduced chromosomal I-Sce I sites in 3T3 cells and have found that they are recombinogenic, stimulating gene targeting two to three orders of magnitude. However, they are also repaired efficiently by end-joining mechanisms (Rouet P et al, Mol Cell Biol, in press). Results of these studies were presented. It is expected that expression of rare-cutting endonucleases in mammalian cells will provide a powerful tool for the analysis of the repair of chromosomal DSBs, as well as for molecular genetic manipulations, such as chromosome fragmentation and, potentially, gene-targeting.

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FILE 'MEDLINE, AGRICOLA, CANCERLIT, SCISEARCH, CAPLUS, BIOSIS, MEDICONF' ENTERED AT 13:09:45 ON 22 APR 2002 756977 S CHROMOSOME? 1.1 L2

301 S L1 AND (INTRON? (L) ENDONUCLEASE?)

137 DUP REM L2 (164 DUPLICATES REMOVED) 1.3

137 FOCUS L3 1-

=> d an ti so au ab pi 14 1, 7

ANSWER 1 OF 137 CAPLUS COPYRIGHT 2002 ACS

1994:318316 CAPLUS AN

DN 120:318316

Thermostable sequence-specific endonucleases of Desulfurococcus and ΤI Pyrobaculum, genes encoding them, and their use in gene analysis and

SO PCT Int. Appl., 73 pp. CODEN: PIXXD2

IN Dalgaard, Jacob Zeuthen; Garrett, Roger Antony; Kjems, Joergen

Thermostable sequence-specific DNA endonucleases are encoded by AΒ archael type introns of stable RNA (rRNA or tRNA) or protein genes or are enzymically active variants thereof in which one or more amino acid residues have been deleted, inserted or substituted by other amino acids. These endonucleases recognize relatively long sequences of about 20 base pairs and are very rare cutters, cleaving with a frequency of about 1:5,000,000. Thus, they are useful as endonuclease tools for gene anal., such as genome mapping and detection of major rearrangements in large genomes, and for gene manipulation, such as cloning and chromosome targeting. Two protein-encoding introns were discovered in the 23S rRNA-encoding gene of P. organotrophum. The RNA products circularize after excision from the 23S rRNA and are stable in the cell. The putative proteins encoded by the introns contain a common decapeptide sequence which is shared by the putative proteins encoded by both the archael intron of D. mobilis and many group I introns. The intron of D. mobilis was shown to encode an endonuclease, the active form of which could be expressed from the linear or cyclized intron, but not from the pre-rRNA. Endonucleases from P. organotrophum (I-Por I) and from D. mobilis (I-Dom I) were produced with recombinant Escherichia coli and their homing/cleavage sites detd.

PATENT NO. KIND DATE PATENT NO. APPLICATION NO. DATE -----

Al 19940303 WO 9404663 PΤ WO 1993-DK264 19930813

W: AT, AU, BB, BG, BR, BY, CA, CH, CZ, DE, DK, ES, FI, GB, HU, JP, KP, KR, KZ, LK, LU, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SK, UA, US, VN

RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

ANSWER 7 OF 137 MEDLINE L4

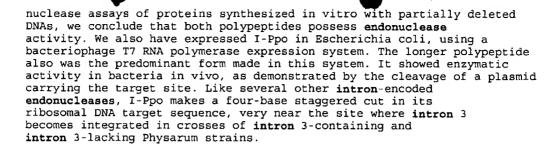
AN 90287128 MEDLINE

Characterization of I-Ppo, an intron-encoded ΤI endonuclease that mediates homing of a group I intron in the ribosomal DNA of Physarum polycephalum.

MOLECULAR AND CELLULAR BIOLOGY, (1990 Jul) 10 (7) 3386-96. SO Journal code: NGY; 8109087. ISSN: 0270-7306.

AU Muscarella D E; Ellison E L; Ruoff B M; Vogt V M

AB A novel and only recently recognized class of enzymes is composed of the site-specific endonucleases encoded by some group I introns. We have characterized several aspects of I-Ppo, the endonuclease that mediates the mobility of intron 3 in the ribosomal DNA of Physarum polycephalum. This intron is unique among mobile group I introns in that it is located in nuclear DNA. We found that I-Ppo is encoded by an open reading frame in the 5' half of intron 3, upstream of the sequences required for self-splicing of group I introns. Either of two AUG initiation codons could start this reading frame, one near the beginning of the intron and the other in the upstream exon, leading to predicted polypeptides of 138 and 160 amino acid residues. The longer polypeptide was the major form translated in vitro in a reticulocyte extract. From



| L Number | Hits | Search Text                                   | DB                     | Time stamp       |
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| 1        | -    | encoded)                                      | US-PGPUB;              |                  |
|          |      |   | EPO; JPO;              |                  |
|          |      |   | DERWENT;               |                  |
|          |      | , ,,,   | USOCR<br>USPAT;        | 2002/04/22 13:53 |
| 8        | 11   | ((group ADJ I ADJ Intron)or (intron ADJ       | US-PGPUB;              | 2002/04/22 13:33 |
|          |      | encoded)) and (chromosome\$2 NEAR mammal\$10) | EPO; JPO;              |                  |
|          |      |   | DERWENT;               |                  |
|          |      |   | USOCR                  |                  |
| 15       | 17   | ((group ADJ I ADJ Intron)or (intron ADJ       | USPAT;                 | 2002/04/22 13:58 |
| 1 2      | 17   | encoded)) and I-sceI\$5                       | US-PGPUB;              |                  |
|          |      |   | EPO; JPO;              |                  |
|          |      |   | DERWENT;               |                  |
| 1        |      |   | USOCR                  | 0000/04/02 13.59 |
| 22       | 10   | DUJON-BERNARD                                 | USPAT;                 | 2002/04/22 13:58 |
|          |      |   | US-PGPUB;<br>EPO; JPO; |                  |
|          |      | ,   | DERWENT;               |                  |
|          |      |   | USOCR USOCR            |                  |